

This Page Is Inserted by IFW Operations  
and is not a part of the Official Record

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

**IMAGES ARE BEST AVAILABLE COPY.**

**As rescanning documents *will not* correct images,  
please do not report the images to the  
Image Problem Mailbox.**

CLAIMS

1. A method for therapeutically treating a tetracycline resistant cell with tetracyclines, which comprises the steps of administering to the cell a predetermined quantity of at least a first composition selected from the chemical group consisting of a blocking agent which is capable of interacting with a product of at least one tetracycline resistance determinant capable of protecting ribosomes in the cell from tetracycline's inhibitory activity; and

concomitantly administering to the cell a predetermined quantity of at least a second composition selected from the chemical group consisting of tetracycline, tetracycline analogues, and tetracycline derivatives which are not said blocking agent.

2. A method according to claim 1 wherein said blocking agent contains a sufficient part of tetracycline to interact with a product of at least one tetracycline resistance determinant capable of protecting ribosomes in the cell from tetracycline's inhibitory activity.

3. A method according to claim 1 wherein said first composition is present in a subinhibitory amount.

4. A method according to claim 1 wherein said tetracycline resistance determinant belongs to the Class A, B, K, L, M, O or Q tetracycline resistance determinant.

5. A method according to claim 1 wherein said blocking agent and said second composition are employed in a molar ratio of from about 0.01 to 100.

6. A method according to claim 1 wherein said blocking agent is also effective against a tetracycline efflux system.

7. A method according to claim 1 wherein said second composition is minocycline, doxycycline, methacycline, demeclocycline, oxytetracycline, or chlortetracycline.

8. A method for converting tetracycline resistant bacteria into tetracycline sensitive bacteria, comprising contacting the

resistant bacteria with a predetermined quantity of at least a first composition selected from C5 esters of tetracycline, 13,5 derivative or 6-deoxy-13-(substituted mercapto)tetracyclines, and concomitantly administering to the cell a predetermined quantity of at least a second composition selected from a tetracycline, a tetracycline analogue or a tetracycline derivative which is not a C5 ester of tetracycline nor a 6-deoxy-13-(substituted mercapto)tetracycline.

9. A method according to claim 8 wherein said first composition is a 6-deoxy-13-(alkyl substituted mercapto)tetracycline.

10. A method according to claim 8 wherein said first composition is a 6-deoxy-13-(aryl substituted mercapto)tetracycline.

11. A method according to claim 8 wherein said first composition is a C5 ester.

12. A method according to claim 8 wherein said first composition is a 13,5 derivative.

13. A method according to claim 8 wherein said second composition is tetracycline.

14. A method according to claim 8 wherein said second composition is minocycline, doxycycline, methacycline, demeclocycline, oxytetracycline, or chlortetracycline.

15. A pharmaceutical preparation for converting tetracycline resistant bacteria into tetracycline sensitive bacteria comprising a blocking agent which is capable of interacting with a product of at least one tetracycline resistance determinant capable of protecting ribosomes in the cell from the inhibitory activity of tetracycline, a tetracycline type antibiotic, and a pharmaceutical carrier.

16. A pharmaceutical preparation according to claim 15 wherein the tetracycline-type antibiotic is a tetracycline, a tetracycline analogue or a tetracycline derivative.

17. A pharmaceutical preparation according to claim 15 wherein said tetracycline resistance determinant belongs to the Class A, B, K, L, M, O or Q tetracycline resistance determinants.

18. A pharmaceutical preparation according to claim 15 wherein the tetracycline-type antibiotic is selected from minocycline, doxycycline, methacycline, demeclocycline, oxytetracycline, or chlortetracycline.

19. A pharmaceutical preparation for converting tetracycline resistant bacteria into tetracycline sensitive bacteria comprising a 6-deoxy-13(substituted mercapto)tetracycline, a tetracycline-type antibiotic which is not a 6-deoxy-13-(substituted mercapto)-tetracycline, and a pharmaceutically acceptable carrier.

20. A pharmaceutical preparation for converting tetracycline resistant bacteria into tetracycline sensitive bacteria comprising a C5 ester of tetracycline, a tetracycline-type antibiotic which is not a C5 ester of tetracycline, and a pharmaceutically acceptable carrier.

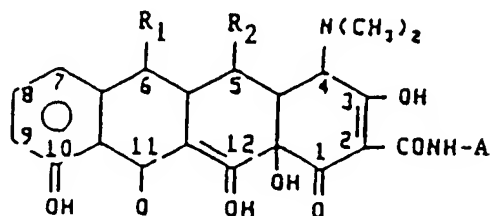
21. A pharmaceutical preparation for converting tetracycline resistant bacteria into tetracycline sensitive bacteria comprising a 13,5 derivative of tetracycline, a tetracycline-type antibiotic which is not a 13,5 derivative of tetracycline, and a pharmaceutically acceptable carrier.

22. A pharmaceutical preparation according to claim 15 wherein the tetracycline-type antibiotic is a tetracycline, a tetracycline analogue or a tetracycline derivative.

23. A pharmaceutical preparation according to claim 15 wherein the tetracycline-type antibiotic is selected from minocycline, doxycycline, methacycline, demeclocycline, oxytetracycline, or chlortetracycline.

24. A class of C5 esters of tetracycline compositions useful in combination with other classes of tetracyclines, tetracycline

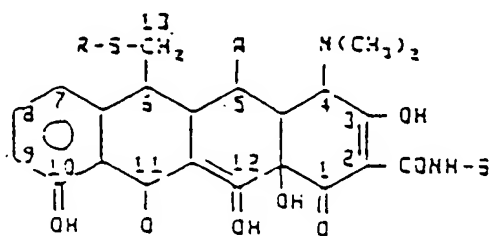
analogues and tetracycline derivatives, said class of compositions having the formula



wherein R<sub>1</sub> and R<sub>2</sub> are selected from the group consisting of a methylene group, hydroxyl, hydrogen or a group consisting of organic entities comprising from 1-12 carbon atoms, with or without other heteroatoms including sulfur, oxygen, halogen, nitrogen, and the like, and takes form as linear, branched, or cyclic alkyl, aryl, or alkylaryl structures; and A is selected from the group consisting of a hydrogen atom, a methylene group, and any linear, branched, or ring structure comprising from 1-6 carbon atoms and optionally including heteroatoms such as oxygen and nitrogen atoms.

25. The compositions of claim 24, wherein the compositions are selected from the group of Formula II, wherein R<sub>1</sub> is CH<sub>3</sub>, H and R<sub>2</sub> is COCH<sub>2</sub>CH<sub>3</sub>, R<sub>1</sub> is =CH and R<sub>2</sub> is COCH<sub>2</sub>CH<sub>3</sub>, R<sub>1</sub> is -CH<sub>2</sub>-S-cyclopentyl, H and R<sub>2</sub> is COCH<sub>2</sub>CH<sub>3</sub>, or R<sub>1</sub> is -CH<sub>2</sub>-S-propyl and R<sub>2</sub> is COCH<sub>2</sub>CH<sub>3</sub>.

26. A class of 6-deoxy-13-(substituted mercapto) tetracycline compositions useful in the therapeutic treatment of a tetracycline resistant cell in combination with other classes of tetracyclines, tetracycline analogues and tetracycline derivatives, said class of compositions having the formula



wherein A is hydrogen or hydroxyl,

B comprises a morpholino group, and

R is an organic entity comprising 1-12 carbon atoms and optionally including heteratoms.

27. A tetracycline composition according to claim 26 having the formula

